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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/089,776	06/21/2002	Kei Tashiro	29288.5600	2614

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EXAMINER	
HAQ, SHAFIQUL	
ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 06/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/089,776	TASHIRO ET AL.	
	Examiner	Art Unit	
	Shafiqul Haq	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 6/13/05, 7/28/04, 6/9/04, 3/5/04 & 2/13/04
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Specification

1. The abstract of the disclosure is objected to because formula (I) of the fluorescent structural portion is missing. Correction is required. See MPEP § 608.01(b).

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Although specific claims may be discussed in the rejections below, these rejections are also applicable to all other claims in which the noted problems/language occur.

4. Claims 1-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5. In claims 1 and 3, "R" is bonded to either sides i.e. not depicted as a terminal group. However, to form a covalent bond with a protein, the functional group "R" needs to be a terminal group. Therefore, its not clear how "R" not being a terminal group, can react with a protein to form a covalent linkage.

6. In claim 1 and 16, the valency of carbon is incorrect for " $-C_nF_{2n+1}-X$". When X=F and n=1, the valency of the terminal carbon will exceed (i.e. the terminal carbon atom will be bonded to a carbon atom and four fluorine atoms) more than it can accommodate.

7. Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are washing steps after binding of first antibody, after sample application and binding, after addition of second antibody and before measurement of fluorescence.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 1-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over each of 1) Yuan et al (Anal. Chem. 1998, Vol. 70, No.3, pp. 596-601) or Matsumoto et al (US 5,859,297) and in view of 2) Pennanen et al (Int. J. Immunopharmacol. 1995, Vol. 17, No. 6, pp. 475-480).

The claims of the present application recite a time-resolved fluorescent immunoassay method for detection of cytokine in biological sample using a streptavidin (or avidin)-lanthanide metal ions conjugate.

Yuan et al disclose a time resolved immunoassay method for detection of alpha-fetoprotein in biological sample (serum) (see title and abstract) comprising the following: (a) anti AFP antibody (first antibody) including a portion bound to a solid-phase and a region bindable to AFP; (b) the AFP; (c) a second antibody including a region bindable to the AFP and a portion to which biotin is bound; and (d) a

conjugate including streptovidin (SA) and a fluorescent structure portion (BHHCT) capable to being complexed with a lanthanide metal ion (Eu+3) (see page 597, fig 1 and page 598, fig.2). The fluorescent structure portion of fig.1 (BHHT and BHHCT) anticipate formula (I) and (III) of the present application. Fluorescence is measured after composite is formed on the solid phase and both solid phase measurement and after dissolution measurement are disclosed (page 598, fig.2).

Matsumoto et al. also disclosed time resolved immunoassay method for detection (both solid phase and liquid phase measurement) of alpha-fetoprotein in a sample (see abstract and column 24, lines 15-20). The fluorescent structural portion of formulas (I), (II) and (III) of claims 1, 3 and 4 of the present inventions are disclosed in this reference (see abstract; column 2, formula (1), (2) and (3); column 19, compound (j') and (j)) that are labeled with avidin or streptavidin (column 15, lines 55-62; column 20, lines 63-67) and complexed with lanthanide metal ions (column 5, lines 35-37 and column 25, lines 15-20). The time-resolved fluoroimmunoassy for detection of AFP includes first antibody (anti-human AFP)(column 23, line 29), human AFP (column 23, line 45), a biotinylated second antibody (biotinylated goat anti-rabbit antibody) (column 23, lines 57-58) and a streptavidin-(fluorescent structural portion)-Eu^{+3} complex (SA-BHHCT-Eu^{+3}) (column 23, lines 65-66).

Although Yuan et al and Matsumoto et al. disclose detection of alpha-fetoprotein in biological sample employing streptavidin-(fluorescent structural portion)-lanthanide complex (e.g. SA-BHHCT-Eu^{+3}) in time-resolved fluoroimmunoassay as

claimed in the present applicaiton, but they fail to disclose detection of cytokine in biological fluids using the method.

Pennanen et al disclose detection of cytokine in a sample by time-resolved fluoroimmunoassay comprising primary antibody (first antibody) bound to solid phase (e.g. microtiter strips), biotinylated second antibody and europium labeled streptavidin (see title and page 476, right column, lines 13-48). However, Pennanen et al do not disclose the fluorescent structure portion (BHHCT) of formula (I) and (III) complexed with streptavidin and europium (streptavidin-BHHCT-Eu^{+3}) required as part of the detection system.

Since, detection of cytokine by time-resolved fluoroimmunoassy using lanthanide-streptavidin complex is common and know in the art, it would have been obvious at the time of the invention to a person of ordinary skill in the art to include cytokine as an equivalent analyte for detection in the method of Yuan et al, with the expectation of obtaining a similarly useful detection method for cytokine in a biological sample.

The features of the dependent claims are either specifically described by the references (e.g. for microtiter plate of claim 15, see page 598, lines 49-55, left column and for the "dilution of biological fluid sample" of claim 2, see Yuan et al, right column, lines 8-13) or constitute obvious variations in parameters which are routinely modified in the art (e.g. heat treatment of sample to expose epitopes).

The packaging of components in kit form (claims 16) is a well-known obvious expedient for ease and convenience in assay performance and once a method has

been established, one skilled in the art would clearly consider compiling in a kit format and change/modify different components of the kit to best suit the assay.

Conclusion

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shafiqul Haq whose telephone number is 571-272-6103. The examiner can normally be reached on 7:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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